



**UNITED STATES ENVIRONMENTAL PROTECTION AGENCY**  
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SCIENTIFIC DATA REVIEWS  
EPA SERIES 361

OFFICE OF  
PREVENTION, PESTICIDES  
AND TOXIC SUBSTANCES

**MEMORANDUM**

DATE: 5 MARCH 2008

SUBJECT: **CYMOXANIL**- Nondietary Human Exposure/Risk Assessment for the Use of Cymoxanil Leafy Greens Crop Subgroup 4A, Bulb Vegetables Crop Group 3, Cilantro Leaves, Caneberries (Crop Subgroup 13A), and Leaf Petiole Vegetables, Crop Subgroup 4B.

PC Code: 129106 DP Code: 349397

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**INTRODUCTION**

Under provisions in Section 3 of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, the E. I. du Pont de Nemours and Company and the InterRegional Research Project Number 4 (IR-4) have requested registration of the fungicide cymoxanil for use Leafy Greens Crop Subgroup 4A, Bulb Vegetables Crop Group 3, Cilantro Leaves, Caneberries (Crop Subgroup 13A), and Leaf Petiole Vegetables, Crop Subgroup 4B. This memorandum serves as the RD's assessment of exposure and risk to occupational pesticide handlers (mixers, loaders, applicators) and to agricultural workers.

The risk assessment techniques used in this document are those that have been developed and refined by the Health Effects Division (HED)/Office of Pesticide Programs' Science Policy Council for Exposure (ExpoSAC). Therefore, the risk assessment methods use herein, are the same as the HED's standard operating procedure (SOP).

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## USE PATTERN SUMMARY

The use pattern summary is taken from Section B of the IR4 request and from draft product labeling for DuPont™ Tanos® Fungicide (EPA Reg. No. 352-604). Tanos® is a dry flowable (DF) formulation which contains 25 % by weight cymoxanil active ingredient (ai).

**The Leafy Green vegetables (Crop Subgroup 4A)** include amaranth, arugula, chervil, edible leaved chrysanthemum, garland chrysanthemum, cilantro, corn salad, garden cress, upland cress, dandelion, dock, endive, lettuce, orach, parsley, garden purslane, winter purslane, radicchio, spinach, New Zealand spinach, and vine spinach.

The target pests are: downy mildew (*Bremia lactucae*, *Peronospora farinosa*), septoria leaf spot (*Septoria spp.*) and white rust (*Allbugo spp.*).

It may be applied aerially, by ground (boom) sprayers and via sprinkler irrigation.

The rate of application ranges from 8 – 10 oz formulation per acre (0.125 – 0.156 lb ai/A). There is a maximum of 48 oz formulation/A/season (0.75 lb ai/A/season). At the high rate of application there could be 5 applications per season.

Ground applications should be made in a minimum of 20 gallons of water per acre (gpa) and aerial applications in a minimum of 5 gpa. Spray volumes should be increased as plants mature to ensure adequate coverage of foliage, blooms and fruit.

Applications should begin prior to the onset of disease. Preventative applications should be made at 5 – 7 day intervals. No more than one application should be made before alternating with another fungicide with a different mode of action.

The preharvest interval (PHI) is 1 day and the restricted entry interval (REI) is 12 hours.

**The Bulb vegetables (Crop Group 3)** include chive, fresh leaves; chive, Chinese fresh leaves; daylily, bulb; elegans, hosta; fritillaria, bulb; fritillaria, leaves; garlic, bulb; garlic, great-headed bulb; garlic, serpent, bulb; kurrat; lady's leek; leek; leek, wild; lily, bulb; onion, Beltsville bunching; onion, bulb; onion, Chinese, bulb; onion, fresh; onion, green; onion, macrostem; onion, pearl; onion, potato, bulb; onion, tree, tops; onion, Welsh; shallot, bulb; shallot, fresh leaves.

The target pests are downy mildew (*Peronospora destructor*), purple blotch, (*Alternaria porri*) and for disease suppression of bacterial soft rot (*Erwinia spp.*) and xanthomonas blight (*Xanthomonas spp.*).

The rate of application, method of application, dilution rate, frequency and timing of application and REI are the same as described above for leafy green vegetables. The PHI is 3 days.

**Caneberries (Crop Subgroup 13A)** include: blackberries, black and red raspberries, loganberries, wild raspberries and cultivars and hybrids of these.

For disease suppression, the target pests are anthracnose (*Elsinoe veneta*), pseudomonas blight (*Pseudomonas syringae*) and spur blight (*Didymella applanata*).

The rate of application is 6 – 10 oz formulation/A (0.094 – 0.156 lb ai/A). It may be applied aerially or by ground equipment. There is a maximum of 72 oz formulation/A/season (1.125 lb ai/A/season). At the high rate of application, that equates to 7 applications/season. The other application parameters are the same as for leafy green vegetables. The PHI is 0 days. Caneberries may also be treated with airblast sprayers.

**The Leaf Petiole Vegetables (Crop Subgroup 4B)** include: cardoon; celery; celery, Chinese; celtuce; fennel; Florence; rhubarb; Swiss chard.

The target pests are: downy mildew (*Peronospora farinosa*, *P. jaapiana*) septoria leaf spot (Late Blight) (*Septoria spp.*).

It may be applied aerially, by ground (boom) sprayers and via sprinkler irrigation.

The rate of application ranges from 8 – 10 oz formulation per acre (0.125 – 0.156 lb ai/A). There is a maximum of 48 oz formulation/A/season (0.75 lb ai/A/season). At the high rate of application there could be 5 applications per season.

Ground applications should be made in a minimum of 20 gallons of water per acre (gpa) and aerial applications in a minimum of 5 gpa. Spray volumes should be increased as plants mature to ensure adequate coverage of foliage, blooms, and fruit.

Applications should begin prior to the onset of disease. Preventative applications should be made at 5 – 7 day intervals. Not more than one application should be made before alternating with another fungicide with a different mode of action.

The preharvest interval (PHI) is 1 day and the restricted entry interval (REI) is 12 hours.

See Table 1.0 for a summary of the proposed new use patterns.

<b>Table 1.0 Summary of Proposed Use Pattern for Cymoxanil</b>	
Formulation	Tanos <sup>®</sup> Fungicide; EPA Reg. No. 352 -604; dry flowable; 25 % ai cymoxanil
Crop/Site	Leafy green vegetables crop subgroup 4A Bulb vegetables, crop group 3 Caneberry crop subgroup 13A Leaf Petiole Vegetables Crop Subgroup 4B
Pest	downy mildew ( <i>Bremia lactucae</i> , <i>Peronospora farinosa</i> ), septoria leaf spot ( <i>Septoria spp.</i> ), white rust ( <i>Allbugo spp.</i> ), downy mildew ( <i>Peronospera destructor</i> ), purple blotch, ( <i>Alternaria porri</i> ) and for disease suppression of bacterial soft rot ( <i>Erwinia spp.</i> ) and xanthomonas blight ( <i>Xanthomonas spp.</i> ) and for anthracnose ( <i>Elsinoe veneta</i> ), pseudomonas blight ( <i>Pseudomonas syringae</i> ) and spur blight ( <i>Didymella applanata</i> )
Method of Applic.	Aerial, ground boom, sprinkler irrigation, airblast
Max. Applic. Rate	10.0 oz formulation/A (0.156 lb ai/A)
Max. No. Applications	5/yr at the high rate except for caneberries which may have 7 applications/yr
Max. Am't/Yr	48 oz formulation/A/season (0.75 lb ai/A/season) except for caneberries which have a maximum of 72 oz formulation/A/season (1.125 lb ai/A/season)
Applic. Interval	5-7 days
Preharvest Interval	Leafy green vegetables 1 day Bulb vegetables 3 days Caneberry 0 days Leaf Petiole Vegetables 1 day
Restricted Entry Interval	12 hours
Manufacturer	du Pont

### OCCUPATIONAL PESTICIDE HANDLER EXPOSURE

Based upon the proposed use pattern, ARIA/RD believes the most highly exposed occupational pesticide handlers will be 1) mixer/loaders using open-pour loading of a dry flowable formulation, 2) applicators using open-cab ground-boom sprayers, 3) applicators using open-cab airblast sprayers, and 4) aerial applicators.

Occupational pesticide handlers may also be exposed while preparing sprinkler irrigation systems for use as an application vehicle. ARIA/RD believes such activities are similar to those of a mixer/loader supporting aerial applications (i.e., preparing batch solutions to, in this case, be metered into an irrigation system's stream). Therefore, a separate assessment for persons preparing solutions for use in an irrigation system is not presented.

RD also believes occupational handlers will be exposed to short-term duration exposures (1 - 30 days). Although multiple applications are likely, they are not expected to be consecutive applications and should be alternated with other fungicides with differing modes of action. The treatment interval is 5 - 7 days. It is unlikely that handlers would

be exposed continuously for 30 or more days (i.e., intermediate-term exposure). Therefore, only short-term duration risks were assessed.

Private (i.e., grower) applicators may perform all functions, that is, mix, load and apply the material. The ExpoSAC SOP Number 12 (29 March 2000) directs that although the same individual may perform all those tasks, they shall be assessed separately. The available exposure data for combined mixer/loader/applicator scenarios are limited in comparison to the monitoring of these two activities separately. These exposure scenarios are outlined in the Pesticide Handler Exposure Database (PHED) Surrogate Exposure Guide (August 1998). HED has adopted a methodology to present the exposure and risk estimates separately for the job functions in some scenarios and to present them as combined in other cases. Most exposure scenarios for hand-held equipment (such as hand wands, backpack sprayers, and push-type granular spreaders) are assessed as a combined job function. With these types of hand held operations, all handling activities are assumed to be conducted by the same individual. The available PHED and other exposure data support this and HED presents them in this way. Conversely, for equipment types such as fixed-wing aircraft, ground-boom tractors, or air-blast sprayers, the applicator exposures are assessed and presented separately from those of the mixers and loaders. By separating the two job functions, HED/RD determine the most appropriate levels of personal protective equipment (PPE) for each aspect of the job without requiring an applicator to wear unnecessary PPE that might be required for a mixer/loader (e.g., chemical resistant gloves may only be necessary during the pouring of a liquid formulation).

No chemical specific data were available with which to assess potential exposure to pesticide handlers. The estimates of exposure to pesticide handlers are based upon surrogate study data available in the PHED (v. 1.1, 1998). For pesticide handlers, it is HED standard practice to present estimates of dermal exposure for "baseline" that is, for workers wearing a single layer of work clothing consisting of a long-sleeved shirt, long pants, shoes plus socks and no protective gloves as well as for "baseline" **and the use of protective gloves** or other PPE as might be necessary. The product label directs applicators and other handlers to wear long-sleeved shirt, long pants, shoes plus socks and chemical-resistant gloves in Category A (such as butyl rubber, natural rubber, neoprene rubber or nitrile rubber), all  $\geq 14$  mils.

The toxicological factors used in this assessment are taken from: Memo, D. Rate et al., 17 May 2007; "Amended (2): Human Health Risk Assessment for Cymoxanil for New Section 3 Uses in/on Grapes (East of the Rocky Mountains), Hops, Dried Cones and Caneberry Subgroup 13A. PC Code 129106. DP Num: 340367".

Cymoxanil is classified in Acute Toxicity Category III for acute dermal toxicity and in Category IV for acute inhalation, primary eye irritation and primary skin irritation. It is not a dermal sensitizer. Relevant to this assessment, the HIARC identified dermal and inhalation toxicological endpoints for use in risk assessments. The short-term (1 -30 days) dermal toxicological endpoint has a No Observable Adverse Effect Level (NOAEL) of 4.0 mg a.i./kg bw/day. The endpoint was identified from a developmental

toxicity study in the rabbit. The effects seen were increased skeletal malformations of the cervical and thoracic vertebrae and ribs and cleft palate. A dermal absorption factor of 7.5 % was identified for use in exposure assessment to convert oral doses to dermal equivalents. .

The short-term inhalation toxicological NOAEL is also 4.0 mg a.i./kg bw/day and also based on the developmental toxicity study in the rabbit. The toxic effects cited are the same as those for the dermal NOAEL. RD assumes 100 % absorption via the inhalation route of exposure. Since the toxic effects were identified from a developmental study with fetal effects, a 60 kg body weight is used for risk calculations.

Cymoxanil is classified as "not likely" to be a human carcinogen. Therefore a cancer risk assessment is not necessary. See Table 2.0 for a summary of exposures and risks to occupational pesticide handlers. See the ATTACHMENT for a summary of toxicological endpoints for use in risk assessment.

<b>Table 2.0 Summary of Exposure &amp; Risk to Occupational Handlers From Cymoxanil</b>				
<b>Unit Exposure<sup>1</sup></b> mg ai/lb handled	<b>Applic. Rate<sup>2</sup></b> lb ai/unit	<b>Units Treated<sup>3</sup></b>	<b>Avg. Daily Exposure<sup>4</sup></b> mg ai/kg bw/day	<b>MOE<sup>5</sup></b>
<b><i>Mixer/Loader - Dry Flowable - Open Pour</i></b>				
Dermal: SLNoGlove 0.066 LC SLWithGlove 0.066 HC Inhal. 0.00077 HC	0.156 lb ai/A	350 A/day	Dermal: SLNoGlove 0.0045 SLWithGlove 0.0045 Inhal. 0.0007	No Glove 770 With Glove 770
<b><i>Applicator - Ground-boom - Open-cab</i></b>				
Dermal: SLNoGlove 0.014 HC SLWithGlove 0.014 MC Inhal. 0.00074 HC	0.156 lb ai/A	200 A/day	Dermal: SLNoGlove 0.00055 SLWithGlove 0.00055 Inhal. 0.00039	No Glove 4,300 With Glove 4,300
<b><i>Applicator - Air-blast - Open Cab</i></b>				
Dermal: SLNoGlove 0.36 HC SLWithGlove 0.24 MC Inhal. 0.0045 HC	0.156 lb ai/A	40 A/day	Dermal: SLNoGlove 0.0028 SLWithGlove 0.0019 Inhal. 0.00047	No Glove 1,200 With Glove 1,690
<b><i>Aerial Applicator (Pilots not required to wear gloves)</i></b>				
Dermal: SLNoGlove 0.0050 MC Inhal. 0.000068 MC	0.156 lb ai/A	350 A/day	Dermal: SLNoGlove 0.00034 Inhal. 0.000062	No Glove 10,000

1. Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from The Pesticide Handler Exposure Database Version 1.1, August 1998. Dermal = Single Layer Work Clothing **No Gloves**; Single Layer Work Clothing **With Gloves**; Inhal. = Inhalation. Units = mg a.i./pound of active ingredient handled. Data Confidence: LC = Low Confidence, MC = Medium Confidence, HC = High Confidence.

2. Applic. Rate. = Taken from IR-4 submission.

3. Units Treated are taken from "Standard Values for Daily Acres Treated in Agriculture"; ExpoSAC SOP No. 9.1. Revised 5 July 2000;

4. Average Daily Dose = Unit Exposure \* Applic. Rate \* Units Treated \* 7.5 % dermal absorption ÷ 60 kg Body Weight

5. MOE = Margin of Exposure = NOAEL ÷ ADD. The NOAELs for short- and intermediate-term dermal and inhalation exposure durations are 4.0 mg a.i./kg bw/day. They are identified from the same developmental toxicity study in the rabbit and cite the same toxic effects. Therefore dermal and inhalation exposures are summed then divided into NOAEL to determine Margin of Exposure.

A MOE of 100 is adequate to protect occupational pesticide handlers from exposures to cymoxanil. The estimated MOEs are all > 100. Therefore the proposed new uses do not exceed ARIA/RD's level of concern.

### POST-APPLICATION EXPOSURE TO AGRICULTURAL WORKERS

It is possible for agricultural workers to have post-application exposure to pesticide residues during the course of typical agricultural activities. HED in conjunction with the Agricultural Re-entry Task Force (ARTF) has identified a number of post-application agricultural activities that may occur and which may result in post-application exposures to pesticide residues. HED has also identified transfer coefficients (TC) ( $\text{cm}^2/\text{hr}$ ) relative to the various activities which express the amount of foliar contact over time, during each of the activities identified. The highest (i.e., most conservative) TC for all the proposed new uses is  $2,500 \text{ cm}^2/\text{hr}$  for hand harvesting or thinning of leafy green vegetables. As a "screening" level assessment, RD herein uses the TC of  $2,500 \text{ cm}^2/\text{hr}$  for hand harvesting or thinning.

The TCs used in this assessment are from an interim TC SOP developed by HED's ExpoSAC using proprietary data from the ARTF database (SOP # 3.1). It is the intention of HED's ExpoSAC that this SOP will be periodically updated to incorporate additional information about agricultural practices in crops and new data on transfer coefficients. Much of this information will originate from exposure studies currently being conducted by the ARTF, from further analysis of studies already submitted to the Agency, and from studies in the published scientific literature.

Lacking compound specific dislodgeable foliar residue (DFR) data, HED assumes 20 % of the application rate is available as dislodgeable foliar residue on day zero after application. This is adapted from the ExpoSAC SOP No. 003 (7 May 1998 - Revised 7 August 2000).

The following convention may be used to estimate post-application exposure.

$$\text{Average Daily Dose (ADD) (mg a.i./kg bw/day)} = \text{DFR } \mu\text{g}/\text{cm}^2 * \text{TC cm}^2/\text{hr} * \text{hr/day} * 0.001 \text{ mg}/\mu\text{g} * 1/60 \text{ kg bw}$$

and where:

$$\text{Surrogate Dislodgeable Foliar Residue (DFR)} = \text{application rate} * 20\% \text{ available as dislodgeable residue} * (1-D)^t * 4.54 \times 10^8 \mu\text{g}/\text{lb} * 2.47 \times 10^{-8} \text{ A}/\text{cm}^2.$$

$$0.156 \text{ lb a.i.}/\text{A} * 0.20 * (1-0)^0 * 4.54 \times 10^8 \mu\text{g}/\text{lb} * 2.47 \times 10^{-8} \text{ A}/\text{cm}^2 = 0.349 \mu\text{g}/\text{cm}^2, \text{ therefore,}$$

$$0.349 \mu\text{g}/\text{cm}^2 * 2,500 \text{ cm}^2/\text{hr} * 8 \text{ hr/day} * 0.001 \text{ mg}/\mu\text{g} * 0.075 (7.5 \% \text{ dermal absorption}) \div 60 \text{ kg bw} = 0.0087 \text{ mg}/\text{kg bw/day}.$$

**MOE = NOAEL ÷ ADD** then  $4.0 \text{ mg/kg bw/day} \div 0.0087 \text{ mg/kg bw/day} = 460$ .

A MOE of 100 is adequate to protect agricultural workers from post-application exposures. The most conservative estimate (i.e., highest exposure/risk) of post-application exposure results in MOEs > 100. Therefore, the proposed risk does not exceed ARIA/RDs level of concern.

#### **RESTRICTED ENTRY INTERVAL (REI)**

Cymoxanil is classified in Acute Toxicity Category III for acute dermal toxicity. It is classified in Toxicity Category IV for acute inhalation toxicity, primary eye irritation and primary skin irritation. It is not a dermal sensitizer. Therefore the interim worker protection standard (WPS) REI of 12 hours is adequate to protect agricultural workers from postapplication exposures to cymoxanil. The Tanos<sup>®</sup> label lists a REI of 12 hours.



## ATTACHEMENT

### Acute Toxicity of Cymoxanil

<b>TABLE 3. Acute Toxicity of Cymoxanil Technical Grade Active Ingredient (TGAI).</b>				
<b>Guideline No.</b>	<b>Study Type</b>	<b>MRID NO.</b>	<b>Results</b>	<b>Toxicity Category</b>
81-1	Acute Oral	43616512	LD <sub>50</sub> = 960 mg/kg	III
81-2	Acute Dermal	43616513	LD <sub>50</sub> > 2000 mg/kg	III
81-3	Acute Inhalation	42706303	LC <sub>50</sub> = >5.06 mg/L	IV
81-4	Primary Eye Irritation	43616514	Non- irritant	IV
81-5	Primary Skin Irritation	43616515	Mild or slight irritant	IV
81-6	Dermal sensitization	43640501	Non sensitizer	N/A

A summary of the toxicological endpoints and doses chosen for the relevant exposure scenarios for human risk assessment is found in Table 5.

<b>Table 5. Updated Summary of Toxicological Doses and Endpoints for Cymoxanil for Use in Human Health Risk Assessments</b>				
<b>Exposure Scenario</b>	<b>Point of Departure</b>	<b>Uncertainty/ FQPA Safety Factors</b>	<b>RfD, PAD, Level of Concern for Risk Assessment</b>	<b>Study and Toxicological Effects</b>
Acute Dietary (General population, including infants and children)	N/A	N/A	N/A	An endpoint of concern (effect) attributable to a single dose was not identified in the database. Quantification of acute risk to general population, including infants and children, is not required.
Acute Dietary (Females 13-49 years of age)	NOAEL = 4 mg/kg/day	UF <sub>A</sub> = 10X UF <sub>H</sub> = 10X  FQPA SF = 1X	aRfD = 0.04 mg/kg/day  aPAD = 0.04 mg/kg/day	<b>Developmental toxicity (rabbit)</b> Offspring LOAEL = 8 mg/kg/day based on increased skeletal malformations of the cervical and thoracic vertebrae and ribs
Chronic Dietary (All populations)	NOAEL < 0.8 mg/kg/day	UF <sub>A</sub> = 10X UF <sub>H</sub> = 10X  FQPA SF <sup>1</sup> = 10X (includes UF <sub>L</sub> = 10X)	cRfD = 0.008 mg/kg/day  cPAD = 0.0008 mg/kg/day	<b>Chronic toxicity (dog; 2003)</b> LOAEL = 1.3/0.8 mg/kg/day (M/F), based on decreased absolute and relative thymus weights and histopathology of the thymus (thymic atrophy/involution) in males and decreased thymus

				weights in females
Incidental Oral Short-Term (1-30 days)	NOAEL = 10.5 mg/kg/day	UF <sub>A</sub> = 10X UF <sub>H</sub> = 10X FQPA SF = 1X	Residential LOC for MOE = 100	<b>2-generation reproduction (rat; 2001)</b> Offspring LOAEL = 31.6/42.8 mg/kg/day (M/F) based on decreased body weight during lactation in both F <sub>1</sub> and F <sub>2</sub> generations
Incidental Oral Intermediate-Term (1-6 months)	NOAEL = 6.5 mg/kg/day	UF <sub>A</sub> = 10X UF <sub>H</sub> = 10X FQPA SF = 1X	Residential LOC for MOE = 100	<b>2-generation reproduction (rat; 1993)</b> Parental LOAEL = 32.1 mg/kg/day (M/F) based on reduced prenatally body weight, body weight gain, and food consumption for P males; and decreased gestation and lactation body weights for F <sub>1</sub> females
Dermal Short-Term (1-30 days)	NOAEL = 4 mg/kg/day  (Dermal absorption = 7.5%) <sup>2</sup>	UF <sub>A</sub> = 10X UF <sub>H</sub> = 10X FQPA SF = 1X	Residential/ Occupational LOC for MOE = 100	<b>Developmental toxicity (rabbit)</b> Offspring LOAEL = 8 mg/kg/day based on increased skeletal malformations of the cervical and thoracic vertebrae and ribs
Dermal Intermediate-Term (1-6 months)	NOAEL = 4 mg/kg/day  (Dermal absorption = 7.5%) <sup>2</sup>	UF <sub>A</sub> = 10X UF <sub>H</sub> = 10X FQPA SF = 1X	Residential/ Occupational LOC for MOE = 100	<b>Developmental toxicity (rabbit)</b> Offspring LOAEL = 8 mg/kg/day based on increased skeletal malformations of the cervical and thoracic vertebrae and ribs
Dermal Long-Term (> 6 months)	NOAEL < 0.8 mg/kg/day  (Dermal absorption = 7.5%) <sup>2</sup>	UF <sub>A</sub> = 10X UF <sub>H</sub> = 10X FQPA SF <sup>1</sup> = 10X (includes UF <sub>L</sub> = 10X)	Residential/ Occupational LOC for MOE = 1000	<b>Chronic toxicity (dog; 2003)</b> LOAEL = 1.3/0.8 mg/kg/day (M/F), based on decreased absolute and relative thymus weights and histopathology of the thymus (thymic atrophy/involution) in males and decreased thymus weights in females
Inhalation Short-Term (1-30 days)	NOAEL = 4 mg/kg/day  (100% inhalation absorption assumed)	UF <sub>A</sub> = 10X UF <sub>H</sub> = 10X FQPA SF = 1X	Residential/ Occupational LOC for MOE = 100	<b>Developmental toxicity (rabbit)</b> Offspring LOAEL = 8 mg/kg/day based on increased skeletal malformations of the cervical and thoracic vertebrae and ribs
Inhalation Intermediate-Term (1-6 months)	NOAEL = 4 mg/kg/day  (100% inhalation absorption assumed)	UF <sub>A</sub> = 10X UF <sub>H</sub> = 10X FQPA SF = 1X	Residential/ Occupational LOC for MOE = 100	<b>Developmental toxicity (rabbit)</b> Offspring LOAEL = 8 mg/kg/day based on increased skeletal malformations of the cervical and thoracic vertebrae and ribs

Inhalation Long-Term (>6 months)	NOAEL < 0.8 mg/kg/day  (100% inhalation absorption assumed)	UF <sub>A</sub> = 10X UF <sub>H</sub> = 10X FQPA SF <sup>1</sup> = 10X (includes UF <sub>L</sub> = 10X)	Residential/ Occupational LOC for MOE = 1000	<b>Chronic toxicity (dog; 2003)</b> LOAEL = 1.3/0.8 mg/kg/day (M/F), based on decreased absolute and relative thymus weights and histopathology of the thymus (thymic atrophy/involution) in males and decreased thymus weights in females
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Abbreviations: UF = uncertainty factor, UF<sub>A</sub> = extrapolation from animal to human (interspecies), UF<sub>H</sub> = potential variation in sensitivity among members of the human population (intraspecies), FQPA SF = FQPA Safety Factor, UF<sub>L</sub> = to account for the use of a LOAEL to extrapolate a NOAEL, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, RfD = reference dose (a = acute, c = chronic), PAD = population adjusted dose, MOE = margin of exposure, LOC = level of concern, N/A = Not Applicable

<sup>1</sup>The 10X FQPA SF has been retained in the form of a UF<sub>L</sub> to account for the use of a LOAEL to extrapolate a NOAEL

<sup>2</sup>An upper-bound estimate calculated as follows by comparing the maternal LOAEL from the oral developmental toxicity study (rat) with the NOAEL from the dermal toxicity study (rat): [(75 mg/kg/day ÷ 1000 mg/kg/day) x 100%] = 7.5%; the last HIARC report of Jan. 2, 2003 incorrectly calculated this to be 2.5%

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13544

**R158348**

**Chemical: Cymoxanil**

**PC Code:  
129106**

**HED File Code: 51200 RD Risk Reviews**

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